UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,750	05/16/2001	Madhavan Nampoothiri K.	32301WD1181	8888

7590 02/21/2003

SMITH GAMBRELL & RUSSELL, L.L.P.
Suite 800
1850 M Street, N.W.
Washington, DC 20036

EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,750	NAMPOOTHIRI K. ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *25,26,31-33 and 40* is/are allowed.

6)☒ Claim(s) *27,28,30,34,36-39 and 41-43* is/are rejected.

7)☒ Claim(s) *29 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/577,848* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. Claims 25-43 are pending in the application.

2. Applicants' cancellation of claims 1-24 and addition of claims 25-43 in Paper No. 12, filed 12/17/02, is acknowledged.

3. Receipt of a computer readable form of the sequence listing and a paper copy thereof in Paper No. 12 is acknowledged.

4. Applicants' arguments presented in Paper No. 12 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

5. The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, Second Paragraph

6. Claims 41-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 41 and 42 are confusing as they depend from cancelled claims 7 and 10, respectively. It is suggested that applicants clarify the meaning of the claims.

b. Claim 43 recites the limitation "the isolated polynucleotide of claim 26". There is insufficient antecedent basis for this limitation in the claim. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

7. The written description rejection of claims 34 and 36-39 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection as it applied to original

claims 1-5, 7-11, 23, and 24 was fully explained in a previous Office action (see item 22 at pages 6-8 of Paper No. 11).

Applicants argue (beginning at page 4 of Paper No. 12) the specification is not required to teach that which is known to those of skill in the art. Applicants argue the specification teaches isolation of the fadD15 gene and the function and amino acid sequence of the encoded polypeptide. Applicants argue the specification teaches microorganisms overexpressing fadD15 are useful for producing L-amino acids. Applicants argue the specification, particularly the Examples describe how to produce the invention and cite well-known articles that allegedly provide additional instruction that is known to a skilled artisan. Applicants argue the newly added claims do not define functionally unrelated polynucleotides and the polynucleotides recited in the newly added claims are adequately described in the specification. Applicants' arguments are not found persuasive.

Claim 34 (in pertinent part) is drawn to a genus of polynucleotides comprising a fragment of SEQ ID NO:1 encoding an acyl-CoA synthase. Claims 36 and 38 are drawn to a genus of polynucleotides comprising at least 15 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, wherein said polynucleotide is a PCR primer for synthesis of a polynucleotide encoding an acyl-CoA synthase or the acyl-CoA synthase of SEQ ID NO:2. Claims 37 and 39 are drawn to a genus of polynucleotides comprising at least 15 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, wherein said polynucleotide is a hybridization probe for isolation of a polynucleotide encoding an acyl-CoA synthase or the acyl-CoA synthase of SEQ ID NO:2. The claims are rejected because the structures of the claimed polynucleotides have not been adequately described in the specification.

Regarding claim 34, the specification teaches only a single representative species of a polynucleotide encoding SEQ ID NO:2, i.e., SEQ ID NO:1. The specification does not disclose any other representative species of polynucleotides *comprising fragments* of SEQ ID NO:1. Regarding claims 36 and 38, the specification discloses only two representative species of PCR primers, i.e., SEQ ID NOs:3 and 4. The specification does not disclose any other representative species of PCR primers *comprising* at least 15 nucleotides SEQ ID NO:1 as encompassed by the claims. Regarding claims 37 and 39, the

specification discloses only a single representative species of hybridization probe, i.e., SEQ ID NO:1. The specification does not disclose any other representative species of hybridization probes comprising at least 15 nucleotides of SEQ ID NO:1 as encompassed by the claims. One of ordinary skill in the art would recognize that there is *substantial variation* within the sequences of the claimed polynucleotides – polynucleotides comprising a fragment of SEQ ID NO:1 (claim 34) and polynucleotides comprising at least 15 nucleotides of SEQ ID NO:1 (claims 36 and 37). When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of the nucleotide sequences of SEQ ID NOs:1, 3, and 4 fails to provide a representative number of species sufficient to describe all members of the claimed genus. Thus, the structures of the claimed genus of polynucleotides have not been adequately described in the specification such that one skilled in the art can reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. The rejection of claims 27, 28, 34, and 36-39 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection as it applied to original claims 1-5, 7-11, 23, and 24 was fully explained in a previous Office action (see item 23 at pages 6-8 of Paper No. 11).

Applicants argue (beginning at page 5 of Paper No. 12) the claims are not so broad as to encompass any bacteria, polynucleotide, primer, or probe and that the specification fully enables the entire scope of claimed bacteria and polynucleotides. Applicants argue that undue experimentation would not be required for a skilled artisan to practice the claimed invention as the specification describes how to produce the entire scope of claimed bacteria and polynucleotides. Applicants' arguments are not found persuasive.

Undue experimentation would be required for a skilled artisan to make the entire scope of claimed bacteria and polynucleotides. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance

presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). The Factors most relevant to the instant rejection are addressed below.

Regarding claims 27 and 28:

- The claims are so broad as to encompass a bacterium comprising a polynucleotide overexpressing, *by any method*, a polynucleotide encoding SEQ ID NO:2, and optionally wherein overexpression is achieved by increasing polynucleotide copy number. The claims are not commensurate in scope with the enablement provided by the instant specification.
- The specification provides enabling guidance in the form of only a single method for overexpressing SEQ ID NO:1, i.e., using an expression vector. While the specification states other methods for overexpression of a polynucleotide, e.g., chromosomal integration and changing media composition (see page 12, paragraph 43 of the instant specification), the specification has provided insufficient guidance to enable a skilled artisan to overexpress a polynucleotide encoding SEQ ID NO:2 by either of these two methods.
- The specification provides only two working examples for overexpressing a polynucleotide encoding SEQ ID NO:2 – Examples 5 and 7. These examples employ a plasmid-based expression system for overexpressing SEQ ID NO:1. These working examples are insufficient to provide enablement for any method of overexpressing SEQ ID NO:1.
- At the time of the invention, a skilled artisan was aware of other methods for overexpression of a polynucleotide as broadly encompassed by the claims. For example, mutations in the endogenous promoter sequence may result in overexpression of a desired gene. However, the instant specification provides insufficient guidance for altering the endogenous promoter of SEQ ID NO:1 for increased expression. Thus, one of skill in the art would be required to isolate the endogenous promoter and determine which mutations, if any, would result in increased expression. One of skill in the art would

recognize the high degree of unpredictability in generating such mutations with an expectation of obtaining the desired effect.

Regarding claims 34 and 36-39:

- The claims are so broad as to encompass all polynucleotides comprising a fragment of SEQ ID NO:1 encoding an acyl-CoA synthase (claim 34), all polynucleotides comprising at least 15 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, wherein said polynucleotide is a PCR primer for synthesis of a polynucleotide encoding an acyl-CoA synthase or the acyl-CoA synthase of SEQ ID NO:2 (claims 36 and 38), and all polynucleotides comprising at least 15 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, wherein said polynucleotide is a hybridization probe for isolation of a polynucleotide encoding an acyl-CoA synthase or the acyl-CoA synthase of SEQ ID NO:2 (claims 37 and 39). The claims are not commensurate in scope with the enablement provided by the instant specification.
- The specification provides guidance in the form of a single working example of polynucleotide comprising a fragment of SEQ ID NO:1, i.e., SEQ ID NO:1, two working examples of PCR primers, i.e., SEQ ID NOs:3 and 4, and a single working example of a hybridization probe, i.e., SEQ ID NO:1. These working examples are insufficient to enable the scope of claimed polynucleotides.
- As stated in a previous Office action, the nucleotide sequence of a polynucleotide determines the encoded protein's structural and functional properties or its ability to function as a PCR primer or hybridization probe. Predictability of which changes can be tolerated in a nucleic acid sequence and obtain the desired activity – in this case encoding a polypeptide with acyl-CoA synthase activity or the ability to prime or hybridize - requires a knowledge of and guidance with regard to which nucleic acids in the sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the structure relates to its function. Furthermore, specifically addressing the polynucleotide of claim 34, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within an encoded protein's

sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any genetically modified coryneform bacteria, polynucleotides, primers, and hybridization probes as described above. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

9. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to be a novel vector. Since the vector is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed vector sequences are not fully disclosed, nor have all the sequences required for its construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the vector. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the vector is readily available to the public. Accordingly, it is deemed that a deposit of this vector should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited a microorganism comprising the novel vector (see paragraph 57 of page 18 of the instant specification) but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or

declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the microorganism has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Fujino et al. (*J Biol Chem* 271:16748-16752). Claim 34 (in pertinent part) is drawn to a polynucleotide comprising a fragment of SEQ ID NO:1 encoding an acyl-CoA synthase. Fujino et al. teach a polynucleotide encoding a polypeptide having acyl-CoA synthetase (synthase) activity (see page 16750). This anticipates claim 34 as written.

Conclusion

11. Claims 27, 28, 30, 34, 36-39, and 41-43 are rejected.

12. Claims 29 and 35 are objected to as being dependent upon a rejected base claim.

13. Claims 27-30, 35-39, and 41-43 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraphs, set forth in this Office action.

14. Claims 25, 26, 31-33, and 40 are in condition for allowance.

The new rejections under 35 USC 112, first paragraph (item 9) and 35 USC 102(b) (item 10) are necessitated by amendment. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600